



Mushrooms Integrative Treatment with *Inonotus obliquus* and *Ganoderma lucidum* in a Triple Negative Breast Cancer Patient: A Case Report

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Abstract

Mycotherapy recently arose in medicine for their health properties. Medicinal mushrooms seem to be useful for immune system modulation and preclinical data show cytotoxicity against breast cancer cells. In this paper, we describe case report of a woman affected by triple-negative breast cancer who used *Inonotus obliquus* and *Ganoderma lucidum* during her treatment.

Keywords: Mycotherapy; *Inonotus obliquus*; *Ganoderma lucidum*; Breast cancer; Integrative oncology

Introduction

The mycotherapy has been successfully used in Asian countries for thousands of years, but in the last decade its use is increasing also in Western medicine, due to its nutritional and health properties, and lately even in integrative oncology [1]. Mushroom extracts contain polysaccharides or polysaccharide-protein complexes, which can modulate the non-specific immune system, displaying an antitumor activity, even in addition to chemotherapeutic regimens [2,3]. These properties are mainly recognized in edible mushrooms such as *Ganoderma Lucidum* (Reishi), *Grifola frondosa* (Maitake), *Schizophyllum commune* (Split Gill) and *Inonotus Obliquus* (Chaga) [4-10]. Recent studies have highlighted the potential activity against cancer cells of the *Inonotus obliquus* extracts, containing terpenes/terpenoids, peptides, sterols, polyphenols and polysaccharides, some of which show a strong cytotoxicity against mouse and human breast cancer cell lines [11,12]. Polysaccharides extracted from *Inonotus obliquus* exhibit potential anti-cancer effects through an antioxidation activity and immune system stimulation [13,14]. Moreover, *Inonotus obliquus* extracts show *in vitro* inhibitor and pro-apoptotic effects against colon cancer and hepatic tumors [15,16]. Despite these preliminary evidences, studies confirming beneficial effects of this mushroom in the clinical setting are still lacking. In our study, we report the first case of successful use of *Inonotus obliquus* in a 49 years old female patient affected by triple-negative breast cancer, which shows an aggressive behavior and a unique molecular profile [17]. This report could pave the path to a broader clinical use of medical mushrooms in this particular subset of breast cancer patients, whose therapeutic options are currently limited and deeply related to immune system modulation.

Case Presentation

A 49 years old female Caucasian patient was recruited at the Center for Integrative Oncology of Gemelli University Polyclinic Foundation IRCCS in Rome.

The patient was affected by an invasive ductal carcinoma of the left breast, grade 3. The results of immunohistochemistry analysis showed a triple negative cancer with a high proliferation index (Ki67 55%).

The patient underwent a left breast mastectomy plus axillary dissection followed by chemotherapy regimen, consisting of 6 cycles of Carboplatin and Paclitaxel. At pathologic examination, the lesion

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was 1 cm, 9 cm in size, while 1 out of 8 lymph nodes removed were positive. No evidence of distant metastasis was found at systemic evaluation through CT scan.

Protocol

Following chemotherapy, and after six days from the beginning of her radiation therapy on residual breast, the patient followed our integrative protocol, including two medicinal mushrooms extracts for one month. The first medication is a syrup containing *Ganoderma lucidum* (Reishi) concentrated extract, the second is a drink containing *Inonotus obliquus* (Chaga) extract, equivalent to 0%, 125% of fresh mushroom. The patient had to take Reishi at the dose of 10 ml after breakfast and Chaga at the dose of 20 ml after lunch. The treatment was very well tolerated and no side effect recorded.

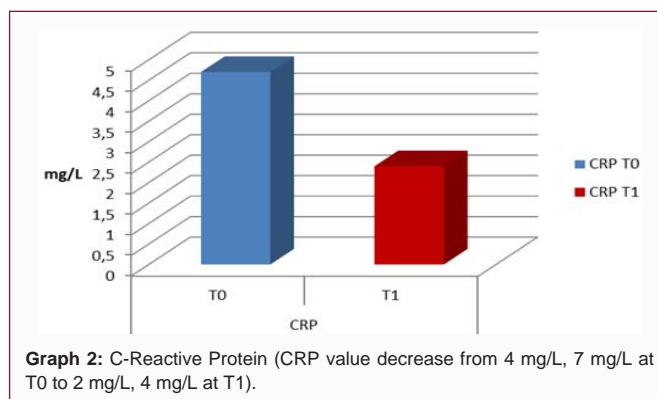
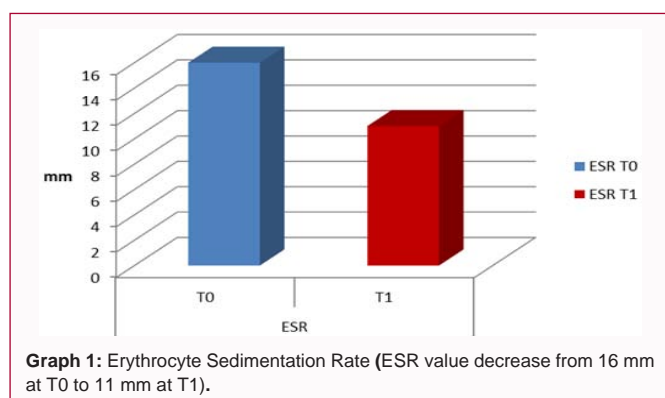
For the present study, the patient underwent blood analyses, including Serum Protein Electrophoresis (SPE), liver enzymes (Aspartate aminotransferase (AST/GOT), Alanine aminotransferase (ALT/GPT), and gamma-Serum Gamma-Glutamyl-Transferase (GGT)), Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP) and Alkaline Phosphatase (ALP). These tests were performed at time zero, before the beginning of integrative therapy, and after 30 days.

Results

After one month of medicinal mushrooms were observed a decrease in ESR value, from 16 mm at T0 to 11 mm at T1 and CRP value from 4 mg/L, 7 mg/L at T0 to 2 mg/L, 4 mg/L at T1 and a slight improvement in SPE despite the fact that patient was receiving radiation therapy at that time (Graph 1 and 2). All the blood values including SPE are reported in supplemental materials.

Discussion

Medicinal mushrooms have been used in traditional Chinese medicine for a large variety of human diseases during the last two thousand years [18]. Mushroom extracts contain a variety of nutritive substances such as polysaccharides (glucans), sesquiterpenes, glycoproteins, peptide/protein-bound polysaccharide, vitamins, amino acids and other organic compounds, which seem to confer health benefits on human beings [1]. The beneficial effects of these molecules are linked to numerous biological properties: They are able to modulate immune system, inhibit cancer growth, function as radical scavengers, detoxify the organism and contribute to cell renewal [2,3,19]. For these reasons, the attention of scientific community toward medical mushrooms is increasing in recent years and has lately been focused on fungal polysaccharides, because they display an immunomodulatory and anticancer activity and seem to



prevent cancer metastasis [19].

In a case report, Cheuk et al. [20] described the regression of a gastric large B-Cell lymphoma in a 47 years old man, who had taken high doses of *Ganoderma lucidum* (Lingzhi). The authors supposed an immunomodulatory effect, due to *Ganoderma lucidum* intake, through cytotoxic T cells host-immune response.

Recent studies have highlighted the anticancer activity of *Ganoderma lucidum* extracts in breast cancer: In particular, they seem to be able to improve tumor control in combination with Paclitaxel in a murine breast cancer model [6]. In addition, Barbieri et al. [5] demonstrated that *Ganoderma lucidum* extracts have anti-inflammatory and anticancer properties in triple-negative breast cancer and melanoma cell lines. Martínez et al. [21] reported that *Ganoderma lucidum* inhibits cell invasion, decreases the gene expression involved in cancer cell survival, proliferation and invasion in inflammatory breast cancer cells. Another study found that *Ganoderma lucidum* extracts show an anti-cancer activity towards triple negative Breast Cancer Stem Cells (BCSCs) through the down-regulation of the STAT3 pathway [22].

Moreover, *Ganoderma lucidum* extracts were shown able to inhibit the release of IL-8, IL-6, matrix metalloproteinase-2 and 9 (MMP-2 and MMP-9), exerting anti-inflammatory and anti-metastatic actions in melanoma and triple-negative breast cancer cells, under pro-inflammatory conditions [5].

A few researches have highlighted the anti-inflammatory effect and anticancer activity of *Inonotus obliquus* (Chaga) extracts. The anti-inflammatory properties seem to be due to the suppression of nitric oxide, the inhibition of cyclooxygenase-2 expression in macrophages and the reduction of oxidative stress in lymphocytes [23-25]. Moreover, some compounds extracted from Chaga may exhibit a strong cytotoxic effect in mouse and human cancer cell lines and in human prostatic and breast carcinoma cell lines [12,23].

In another study, extracts from *Inonotus obliquus* inhibited the proliferation of human colon cancer cell lines, probably by promoting apoptosis and suppressing cancer growth through the up-regulation of proapoptotic proteins [15].

To the best of our knowledge, no other paper in the past studied *in vivo* effects of *Inonotus obliquus* on a breast triple negative cancer patient during oncological treatments.

In the present report, we have studied the effects of two types of medicinal mushrooms *Ganoderma lucidum* and *Inonotus obliquus* in a triple negative breast cancer patient, following chemotherapy and during her radiation therapy protocol.

In our case, after a brief period of integrative treatment (one month) and despite the low dosages employed, we observed a stabilization of transaminases, a slight improvement in serum protein electrophoresis and a significant reduction in inflammatory markers (ESR and CRP), even during the radiation therapy, which is a recognized cause of systemic and local inflammation.

Both tolerance and adherence to the protocol were excellent and no side effects were reported by the patient. Our experience confirms the literature observations reported so far, which suggests that integrative evidence based treatments, including medicinal mushrooms, represent a promising approach in cancer patients, in combination with conventional therapies, in order to reduce side effects and improve quality of life.

Conclusion

This study represents an isolated case-report, with several limitations on the clinical interpretation of the results; nevertheless, the optimal tolerance to the treatment with mushrooms, together with their confirmed anti-inflammatory effect, even in a breast cancer patient affected by an aggressive subtype such as a triple negative, might suggest further investigations in this direction, focusing on longer periods of treatments, higher dosages and extended follow-up.

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